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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,958	05/31/2006	Kai Michael Exner	12810-00257-US	9216
23416 7590 04/22/2008 CONNOLLY BOVE LODGE & HUTZ, LLP P O BOX 2207 WILMINGTON, DE 19899				
EXAMINER				
CUTLIFF, YATE KAI RENE				
ART UNIT		PAPER NUMBER		
1621				
MAIL DATE		DELIVERY MODE		
04/22/2008		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/580,958

**Applicant(s)**

EXNER ET AL.

**Examiner**

YATE K. CUTLIFF

**Art Unit**

1621

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11 January 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-946)
- 3) ☐ Information Disclosure Statement(s) (PTO/SG/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Status of Claims***

1. Claims 1-16 are pending.
2. Claims 1-16 are rejected.

### ***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 16 recites the limitation "the catalyst" in line 1. There is insufficient antecedent basis for this limitation in the claim.

### ***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Surmatis, (US 3,932,485), Schulz et al. (US 4,182,731), Pommer et al. (US 3,006,939) and Schleich et al. (US 4,254,281).

9. The rejected claims cover, inter alia, the process for preparing vitamin A acetate of the formula (I) by reacting beta-vinylinol of formula (II) with triphenylphosphine in the presence of sulfuric acid to give C15 salt of the formula (III) with the salt being hydrogen sulfate and/or methylsulfate. **Subsequent to the preparation of the C15 salt, the C15 salt is reacted with C5 acetate of formula (IV) in a Wittig reaction in water as solvent and in the presence of a base to form the vitamin A acetate. The synthesis of C15 salt of formula (III) starts with the beta-vinylionol in a solvent consisting of methanol, water and aliphatic, cyclic or aromatic hydrocarbons having 5 to 8 carbon atoms.** Dependent claims 2-15 are drawn to the work up and optimization of the final product. Dependent claim 16 recites the use of a catalyst mixture which appears to be a species of the solvent mixture of claim 1.

10. Surmatis teaches the process for making the Wittig salt (phosphonium salt) by reacting the triarylphosphine of formula I with an alcohol of formula II-D in the presence of a weak organic base with a strong acid in an inert organic solvent. In Examples 1 and 2, it is disclosed that a mixture of solvents (that includes aliphatic, cyclic or aromatic hydrocarbons) and the acid were first mixed together, then the triphenylphosphine and vinyl-beta-ionol were added all at once. Surmatis states that the Wittig salts are useful for the preparation of vitamin A. (see column 1, lines 7-9).

Surmatis fails to disclose: i) the beta-vinylinol in a solvent mixture of methanol, water and aliphatic, cyclic or aromatic hydrocarbons having 5 to 8 carbon atoms, prior to reacting with the triphenylphosphine in the presence of sulfuric acid, and ii) the Wittig reaction for making the vitamin A acetate.

Schleich et al. discloses the process for manufacturing vitamin A acetate by reacting the salt formed by the reaction of vinyl-beta-ionol (beta-vinylinol) and triphenylphosphine with an aqueous solution of acid selected from sulfuric acid, a bisulfate, phosphoric acid or hydrochloric acid, with a  $\gamma$ -acetoxytiglic aldehyde (C5 acetate) (Wittig reaction). The salt of Schleich et al. is a beta-ionylidenethyltriphenylphosphonium salt (C15 salt). Schleich et al. discloses a Wittig reaction that uses  $\gamma$ -acetoxytiglic aldehyde (C5 Acetate) in the vitamin A acetate process. (see column 1, line 14 - 15). Further, **water is used as the solvent in the vitamin A acetate process of the Wittig reaction.** (see column 1, lines 15 - 22). Additionally, it is stated that the presence of a base is required in the reaction, one such base being ammonia. (see column 1, lines 43 - 45 and line 51).

Schleich et al. fails to disclose that the process for making the beta-ionylidenethyltriphenylphosphonium salt (C15 salt) includes the use of a solvent mixture.

For additional discussions on Surmatis and Schleich, Applicant is directed to the Examiner comments in the Office Action mailed September 12, 2007.

Schulz et al. discloses the process for preparing aqueous solutions of polyenyltriarylphosphonium salts in organic solvents by driving off the solvent with steam, part of the steam being allowed to condense. (see Abstract). Schulz et al. discloses the basic reaction to obtain phosphonium salts which includes the use of solvents, with some of the best yields obtained when methanol is used as a solvent. (see column 1, lines 29-33 and 56-62). Schultz et al. discloses a listing of solvents that have been used in the reaction to make the polyenyltriarylphosphonium salt, this list includes lower aliphatic alcohols and benzene (aromatic with 5-9 carbons) (see column 1, lines 36-44). Schulz et al. states that the reaction process for making phosphonium salts requires a solvent; especially when sulfuric acid is used as the proton donor. (see column 2, lines 14-16). Additionally, the reaction temperature ranges between 30°C to 120°C. (see column 2, lines 36-40). Further, it is disclosed in Example 8 the process of forming phosphonium salt entails a reaction that takes triphenylphosphine adds it to isobutanol and concentrated sulfuric acid, then to this mixture vinyl-beta-ionol was add and water.

Pommer et al. disclose the process for producing beta-cyclogeranylidene series with one such compound being formula VII. Pommer et al. states that starting from a

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beta-ionol it is possible in a single stage to obtain crystalline vitamin A acid or its salts by reacting beta-ionol (VII) in the presence of an organic solvent or **solvent mixture** with a hydrohalide of a triarylphosphine. (see column 3, lines 21-25).

Applicant's claimed invention incorporates the solvent mixture with the beta-vinyionol prior to the addition of the triphenylphosphine and sulfuric acid, in the preparation of the C15 salt of formula III. The prior arts of Surmatis, Schulz and Pommer teach processes for making the polyenyltriarylphosphonium salts, wherein the reaction process uses solvents such as inert organic solvents, alcohols, water and solvent mixtures. The solvents are incorporated in the reaction process in a variety of sequences. Applicant's process for making the salt of formula (III) changes the sequence steps for adding the solvent mixture. The selection of any order of performing process steps is prima facie obvious in the absence of new or unexpected results; In re Gibson, 39 F2d 975, 5 USPQ 230 (CCPA 1930). Selection of any order of mixing ingredients is prima facie obvious.

With regard to the multitude of ranges of solvent mixtures used in the synthesis of the salt of formula (III), Applicant is directed to the Examiner's comments on page 7 of the Office Action mailed September 12, 2007.

For the reasons set forth above and those set out in the Office Action of September 12, 2007, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to prepare a C15 salt of formula (III) as suggested by Surmatis, Schulz and Pommer; then use the salt in a subsequent Wittig reaction where water is the solvent and a base is used as suggested by Schleich et al., which

teaches the use of a beta-ionyildenethyltriphenylphosphonium hydrogen sulfate salt in a Wittig type of reaction to make vitamin A acetate, to produce the vitamin A acetate of formula (I) as set out in Applicant's claimed process with success.

Therefore, all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. *KSR International Co. v. Teleflex Inc.*, 550 U.S. \_\_\_, 82 USPQ2d 1385 (U.S. 2007).

#### ***Response to Amendment***

11. The amendment to claims 1, 2, 5, 7, 8 and 9, and new claim 16 filed January 11, 2008 have been entered.

#### ***Response to Arguments***

12. Applicant's arguments, see page 6, filed January 11, 2008, with respect to claims 2, 5, 7, 8 and 9 have been fully considered and are persuasive. The 112 second paragraph rejection of to claims 2, 5, 7, 8 and 9 has been withdrawn.

13. Applicant's arguments with respect to claims have been considered but are moot in view of the new ground(s) of rejection.

14. Applicant's arguments, see page 8, with respect to claims 1, 5 and 12 have been fully considered and are persuasive. The provisional obviousness-type double patenting rejection of claims 1, 5 and 12 has been withdrawn.



***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to YATE K. CUTLIFF whose telephone number is (571)272-9067. The examiner can normally be reached on M-TH 8:30 a.m. - 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571) 272 - 0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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